Amendments to the Specification

Please replace the paragraph beginning at page 17, line 18, with the following amended paragraph.

Western blot analysis: PC12 cells were plated at 7 x 10^6 cells/T75 flask. After exposure to 4HNE, colostrinin or their combination, cells were collected and lysed in 50 millimolar (mM) Tris, 5 mM EDTA, 150 mM NaCl, 0.5% NP-40, 10% glycerol and protease inhibitor cocktail (supplemented with 1 mM Na_3VO_4, 2 mM EDTA, 1 mM phenylmethylsulfonyl fluoride). Lysates were centrifuged at 14,000g for 10 minutes (min) (4°C) and 40 µg of protein was fractionated on a 10% SDS-polyacrylamide gel and transferred to protein-optimized membranes (Amersham, Inc.). p53 was detected using specific antibody (DO1; Santa Cruz Biotechnology, Inc.) at a dilution of 1:300. Adducts were detected using an antibody to HNE-protein adducts (Pharmingen, Inc.) at a dilution of 1:500. The anti-phospho-JNK antibody (New England Biolabs, Inc., Beverly, MA) was raised against a synthetic phosphopeptide ~~(SFMMT*PY*VVTRYYR)~~ corresponding to residues 179-193 of JNK. For visualization of primary antibody binding, all blots were incubated with horseradish peroxidase-conjugated secondary antibody (Amersham, Inc.) at a dilution of 1:2000, followed by chemiluminescence detection (Amersham, Inc.) and autoradiography.

Please replace the paragraph beginning at page 25, line 15, with the following amended paragraph.

CLN induced differentiation in SH-SY5Y cells in a dose dependant manner ~~(Table 1A)~~ (Table 1). The ability of CLN to induce differentiation in these cells is shown in Figure 6A, the control compared to Figure 6C, a culture treated with 0.1 µg/ml CLN (see figure legends).

Please replace the paragraph beginning at page 25, line 19, with the following amended paragraph.

It has been shown that colostrinin can inhibit the toxicity of Beta-amyloid in neural derived SH-SY5Y cells. Essentially complete inhibition of the toxicity occurred at the 0.01 μg/ml level ~~(Table 1B)~~ (Table 1). Figures 6D and 6E shows the protective effect of 3.0 and 0.1 μg/ml of CLN on B-amyloid induced toxicity as shown in Figure 6B. Since this toxicity is the result of the apoptotic activity of Beta-amyloid (β-amyloid), the data indicate that colostrinin is a potent inhibitor of apoptosis in neural-derived cells. This potent activity indicated that even lower concentrations of colostrinin would have to be tested to determine the potency and anti-apoptotic dose response effect of colostrinin in this system. However, a dose dependant development of differentiation did occur in the presence of Beta-amyloid in the colostrinin treated cells (Figures 6D and 6E).

Please replace the paragraph beginning at page 26, line 15, with the following amended paragraph.

The data reported herein shows the ability of CLN to block the activity of cells treated with 20 μM retinoic acid (the toxicity developed too rapidly in cells treated with 40 μM). ~~Table 1C~~ Table 1 indicates that 1.0 μg/ml of CLN almost completely blocked the cytotoxicity of retinoic acid. The retinoic acid induced differentiation in these cells by day two, but the cells started showing signs of toxicity by day 6. CLN, 1.0 μg/ml, added on day one or for 30 minutes on day five of the experiment completely blocked the toxicity, and similar to the finding with Beta-amyloid, also induced the cells to proliferate. Figures 6F and 6G further document the finding. Figure 6F shows the toxicity induced by retinoic acid compared to Figure 6G, which clearly shows differentiated cells (see legends).